Listings of Claims

1. (Currently Amended): A method of detecting ivermectin sensitivity in a subject, comprising determining whether a gene-truncation mutation in a *mdr1*-encoding sequence of the subject ~~or a truncated P-pg~~ is present in the subject, wherein the gene truncation mutation is a deletion of four base pairs at about residue 294-297 of SEQ ID NO: 1, wherein presence of the gene-truncation mutation ~~or truncated P-gp~~ indicates that the subject is sensitive to ivermectin.

2. (Original): The method of claim 1, wherein the subject is a canine.

3. (Canceled)

4. (Original): The method of claim 1, wherein the method is used to evaluate whether the subject can be treated safely with ivermectin or another drug that can be excluded from a cell or an organ by P-gp.

5. (Original): The method of claim 4, wherein the method is used to evaluate whether the subject can be treated safely with ivermectin or another drug that can be excluded from the brain by P-gp.

6. (Original): The method of claim 1, further comprising determining whether the subject is homozygous or heterozygous for the gene-truncation mutation.

7. (Original): The method of claim 1, wherein determining whether a gene-truncation mutation is present in the subject comprises subjecting DNA or RNA from the subject to amplification using oligonucleotide primers.

8. (Original): The method of claim 6, comprising an oligonucleotide ligation assay.

9. (Original): The method of claim 1, comprising:

obtaining a test sample of DNA containing a *mdr1* sequence of the subject; and

determining whether the *mdr1* sequence of the subject has the gene-truncation mutation in the *mdr1* sequence,

wherein the presence of the mutation indicates sensitivity of the subject to ivermectin.

10. (Currently Amended): The method of claim 9, wherein determining whether the *mdr1* sequence of the subject has the mutation ~~comprising~~ comprises using restriction digestion, probe hybridization, nucleic acid amplification, or nucleotide sequencing.

11. (Currently Amended): The method of claim 1, comprising:

obtaining from the subject a test sample of DNA comprising an *mdr1* sequence;

contacting the test sample with at least one nucleic acid probe for ~~an~~ the *mdr1* gene truncation mutation that is associated with ivermectin sensitivity, to form a hybridization sample;

maintaining the hybridization sample under conditions sufficient for specific hybridization of the *mdr1* sequence with the nucleic acid probe; and

detecting whether the *mdr1* sequence specifically hybridizes with the nucleic acid probe, wherein specific hybridization of the *mdr1* sequence with the nucleic acid probe indicates ivermectin sensitivity of the subject.

12. (Original): The method of claim 10, wherein the probe is present on a substrate.

13. (Original): The method of claim 12, wherein the substrate is a nucleotide array.

14 through 21. (Canceled)

22. (Currently Amended): A kit for use in diagnosing or detecting ivermectin sensitivity in a subject, comprising a probe that specifically hybridizes to an *mdr1* gene-

truncation mutation ~~associated with ivermectin sensitivity~~ at about residue 294-297 of SEQ ID NO: 1.

23 through 26. (Canceled)

27. (Currently Amended): An oligonucleotide that specifically hybridizes to a canine *mdr1* gene-truncation mutation at about residue 294-297 of SEQ ID NO: 1.

28 through 42. (Canceled)

Remarks

Amendments to the Claims

Claims 1-42 were pending in this application. Claims 3, 14-21, 23-26, and 28-42 are canceled by this amendment. Applicants expressly reserve the right to pursue protection of any or all of the canceled subject matter in a subsequent application.

In addition, Claims 1, 10, 11, 22, and 27 are amended herein. Support for the amended language in Claims 1, 22, and 27 can be found at least in Example 1, at page 10, as well as in original Claims 3, 23, and 28, respectively. Claim 10 is amended to correct an obvious typographical error. Claim 11 is amended to reflect the amendment made in Claim 1.

No new matter is introduced by these amendments. After entry of this amendment, **Claims 1, 2, 4-13, 22, and 27 are pending in the application.**

Response to Restriction Requirement

The Restriction Requirement contends that the present application includes claims directed to eight independent and distinct inventions. Applicants herewith cancel Claims 3, 14-21, 23-26, and 28-42, thereby rendering moot the Restriction Requirement as regards Groups II, III, IV, VI, VII and VIII.

Applicants traverse the Requirement as regards Groups I and V, and request that the Examiner recombine the claims in these Groups. In the event the Restriction Requirement is maintained, Applicants provisionally elect Examiner's Group I.

MPEP § 803 requires that two criteria be met before a proper Restriction Requirement can be imposed. These requirements are: (1) that the inventions be independent and distinct as claimed; and (2) that there be a serious burden on the examiner to examine the claims together. Applicants believe that, even assuming Groups I and V are independent and distinct inventions (and Applicants make no such admission), references related to the two groups would be found in a single search and without an undue burden on the Examiner. Therefore, Applicants

respectfully request that the Examiner withdraw the Restriction Requirement as to Groups I and V.

In the words of the Restriction Requirement, the Examiner's Group I is drawn to "a method of detecting ivermectin sensitivity in a subject, comprising determining whether a gene truncation mutations in a mdr1-encoding sequence using nucleic acids, probes, primers, and a nucleotide array." Examiner's Group V is drawn to "kits containing nucleic acids and oligonucleotides that hybridize to the canine mdr-1 gene truncation mutation."

References related to Groups I and V would be found in a single search, and without undue burden on the Examiner

All of the independent claims in Groups I and V now require that the claimed subject matter be used for determining whether a gene-truncation mutation is present in a specified region (at about residue 294-297) of an *mdr1*-encoding sequence (SEQ ID NO: 1). Therefore, a search for references relating to the methods in Group I will lead to the discovery of art relating to the composition in Group V, and vice versa. Because references related to Groups I and V would be found in a single search and without undue burden on the Examiner, Applicants request that the Restriction Requirement be withdrawn as relates to Groups I and V.

Further, the Restriction Requirement does not provide a process of using the nucleic acid of Group V that is materially different from the processes encompassed in Group I of the application

The Restriction Requirement contends that Groups I and V define distinct inventions (product and process of use) because "the product as claimed [in Group V] can be used in a materially different process" from the method claimed in Group I. MPEP § 806.05(h). The example used by the Office to illustrate this position is that "the nucleic acid of invention V can be used in a materially different process such as for sequencing reagents and involving amplification and sequencing methods in order to achieve the objective of genotyping an individual for pedigree analysis." (Office Action, at the top of page 6.)

Applicants respectfully disagree that the Office example in fact defines a materially different process. The process of using the nucleic acid of Group V in the provided example is not materially different from the processes encompassed in Group I of the application. Like the process in the example, the method of Group I comprises nucleic acid hybridization and/or amplification and/or nucleotide sequencing. Even assuming that the objective cited in the Office example (pedigree analysis) is different from the objectives of the method of claims in Group I, the *processes* used (*i.e.*, nucleic acid hybridization and/or amplification and/or nucleotide sequencing) to achieve these objectives are not materially different.

The MPEP places the burden on the Office to provide a materially different process. Because the example in the Restriction Requirement does not contain a process that is materially different from those encompassed in the claims of Group I, Applicants request that the Examiner withdraw the Restriction Requirement between Groups I and V.

Conclusions

In light of the above arguments and for the reasons stated above, Applicants request that the claims of Groups I and V be examined together, and that the requirement for restriction between these groups be withdrawn. However, in the event the Restriction Requirement is maintained, Applicants provisionally elect Group I.

Examiner Sakelaris is invited to telephone the undersigned if any questions remain concerning the requirement for restriction. Otherwise, the present application is ready for substantive examination, and such action is requested.

Respectfully submitted,

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